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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/211,691	12/14/1998	MICHEL GILBERT	14137-129-10	9572

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EXAMINER
RAO, MANJUNATH N

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 08/26/2002 22

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/211,691	GILBERT ET AL.	
	Examiner	Art Unit	
	Manjunath N Rao	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 July 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,5-27 and 33-36* is/are pending in the application.

4a) Of the above claim(s) *13-22 and 36* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,5-12,23-27 and 33-35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claims 1-3, 5-27, 33-36 are still at issue and are present for examination. Claims 1-3, 5-12, 23-27, 33-35 are now under examination. Claims 13-22, 36 remain withdrawn from further consideration as being drawn to non-elected species.

Election/Restrictions

Applicant's election of the species comprising "an isolated nucleic acid that encodes a fusion protein comprising a sialyltransferase and a CMP-sialic acid synthetase" in Paper No. 21 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 13-22, 36 are now withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention, the requirement having been traversed in Paper No. 21.

Applicants' arguments filed on 4-16-02, paper No. 16, have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode

contemplated by the inventor of carrying out his invention.

Claims 1-3, 5-11, 23-27, 33-35 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Enablement requires that the specification teach those in the art to make and use the invention without undue experimentation. Factors to be considered in determining whether a disclosure would require undue experimentation include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The breadth of the claims encompass a polynucleotide encoding a catalytic domain of a glycosyltransferase and a catalytic domain of an accessory enzyme which catalyzes a step in the formation of a nucleotide sugar. However, insufficient examples and guidance are provided on catalytic domains of any glycosyltransferase or said accessory enzymes. The skill of those in the art is low in determining the catalytic domains of an enzyme and the prior art does not teach catalytic domains of a glycosyltransferase or said accessory enzymes. Additionally, by only having the catalytic domains of said enzymes, one of skill in the art would not necessarily know how to use the fusion protein as a protein comprising only the catalytic domain would not necessarily have enzymatic function. Undue experimentation would be required to make and use the invention based upon the instant disclosure.

Claims 1-3, 5-11, 23-27, 33-35 are also rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a polynucleotide which encodes a fusion protein comprising a specifically identified full length glycosyltransferase and a specifically identified full length accessory enzyme, does not reasonably provide enablement for a polynucleotide which encodes a fusion protein comprising any glycosyltransferase and any accessory enzyme which catalyzes a step in the formation of a nucleotide sugar which is a saccharide donor for a glycosyltransferase. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Enablement requires that the specification teach those in the art to make and use the invention without undue experimentation. Factors to be considered in determining whether a disclosure would require undue experimentation include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The breadth of the claims encompass a polynucleotide encoding a fusion polypeptide comprising a catalytic domain of any glycosyltransferase and a catalytic domain of any accessory enzyme which catalyzes a step in the formation of a nucleotide sugar which is a saccharide donor for said glycosyltransferase. Insufficient guidance and working examples are provided of polynucleotides encoding a fusion enzyme comprising a glycosyltransferase and the specific accessory enzyme. One of skill in the art would not know how to make or use a

polynucleotide encoding a fusion enzyme comprising any glycosyltransferase with any accessory enzyme. Without a specific accessory enzyme, one of skill in the art would not know how to make and use the above fusion glycosyltransferase. Similarly, without a specific glycosyltransferase enzyme, one of skill in the art would not know how to make and use the appropriate accessory enzyme. Additionally, the breadth of the claim of an accessory enzyme which catalyzes a step in the formation of a nucleotide sugar encompasses any enzyme involved in any step of biosynthesis of a nucleotide or a sugar. Similarly, the scope of the claim drawn to any glycosyltransferases is too broad encompassing any glycosyltransferases including variants and mutants derived from any source. Insufficient guidance and examples are provided on both the above enzymes which are encompassed by said glycosyltransferases and accessory enzymes. Undue experimentation would be required to enable the full scope of the claims based upon the instant disclosure.

In response to the previous office action comprising the above rejection, applicants have traversed the same arguing that Examples 1 and 2 of the specification exemplify how to make a fusion protein comprising an accessory enzyme and a glycosyltransferase. Applicants argue that they have demonstrated how to successfully make and use two very different enzymes. Applicants argue that they have demonstrated how to choose appropriate accessory enzyme and glycosyltransferase for fusion.

Applicants also argue that one skilled in the art would know how to identify and select an accessory enzyme that catalyzes the formation of the nucleotide sugar and how to identify and select a glycosyltransferase that catalyzes the transfer of a saccharide from a saccharide donor comprising the nucleotide sugar formed by the recited accessory enzyme without undue

experimentation. While this may be so applicants have not taught as which specific pair of glycosyltransferase and accessory enzyme selected from a large number available to one skilled in the art would work efficiently or positively with each other as a fusion protein. Applicants also argue that these enzyme s are highly specific and undue experimentation would not be required.

Examiner respectfully disagrees with the above arguments and also the argument by the applicants that the examples they provide is sufficient to overcome the above rejection. This is because, while Examiner acknowledges that applicants have provided "one" example, they have not specifically shown that one skilled in the art can simply take any glycosyltransferase and any accessory enzyme simply based on the sugar nucleotide of interest and use it to make the fusion protein. Art teaches several types of glycosyltransferases and accessory enzymes with varied levels of activity. Furthermore, it is very well known in the art that the fused form of the enzymes should be "kinetically favorable" with each other depending on the "turnover" rate of each of the enzymes involved in the fusion protein, which in turn depends on the acceptor molecule. Without actual data for all the possible combination of glycosyltransferase and accessory enzymes, it would be undue burden to one skilled in the art to determine which specific glycosyltransferase and which specific accessory enzyme would go to form a perfectly matched pair for a fusion protein with any practical advantage if any. Therefore, Examiner continues to maintain the above rejection.

Claims 1-3, 5-11, 23-27, 33-35 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to

reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. These claims are directed to a genus of DNA molecules encoding a fusion protein comprising any glycosyltransferase and any accessory enzyme. The specification does not contain any disclosure of the structure of all DNA sequences encompassed by the claim. The genus of DNAs that comprise these above DNA molecules is a large variable genus. Therefore, many structurally unrelated DNAs are encompassed within the scope of these claims, including partial DNA sequences. The specification discloses only a single species of the claimed genus which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

In response to the previous Office action, applicants argue that the specification describes the structure and function of the DNAs encoding the enzymes involved in the fusion protein by providing specific page numbers for support. However, a perusal of page 12 and page 23 simply indicates general methods to construct DNA encoding a fusion protein. However there is no information as to specific nucleotide sequences used for construction. Next, applicants also argue that Example 1 describes the construction and expression of DNA encoding a CMP-Neu5Ac synthetase/α 2,3-sialyltransferase activity etc. However, a perusal of example 1 indicates that the fusion protein was made using specifically, polynucleotide sequences

encoding α2,3-glycosyltransferase and CMP-Neu5Ac synthetase isolated from *Neisseria* bacteria. While applicants have provided one specific example that does not constitute a representative example for a DNA encoding a fusion protein comprising all or any glycosyltransferase and all or any accessory enzyme. As discussed in the written description guidelines, the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. A representative number of species means that the species which are adequately described are representative of the entire genus. **Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus.** Satisfactory disclosure of a representative number depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed. For inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus. In the instant case the claimed genera of claims 1-3, 5-11, 23-27, 33-35 includes species which are widely variant in structure and function. The genus claims 1-3, 5-11, 23-27, 33-35 are structurally and functionally diverse as it encompasses polynucleotides from a wide variety of sources and varying levels of activity. As such, neither the description of the structure and

function of a DNA encoding a α2,3-glycosyltransferase and CMP-Neu5Ac synthetase isolated from a single source such as *Neisseria* nor the disclosure solely of functional features present in all members of the genus is sufficient to be representative of the attributes and features of the entire genus. Therefore the above rejection is maintained.

Conclusion

None of the claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Manjunath N Rao whose telephone number is 703-306-5681. The examiner can normally be reached on 7.30 a.m. to 4.00 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy can be reached on 703-308-3804. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-306-0196.

Manjunath N. Rao
August 21, 2002